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EXAMINER	
DEVI, SARVAMANGALA J N	

ART UNIT	PAPER NUMBER
1645	

DATE MAILED: 01/15/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/081,170	KAWAOKA, YOSHIHIRO	
	Examiner	Art Unit	
	S. Devi, Ph.D.	1645	

-- *The MAILING DATE of this communication appears on the cover sheet with the correspondence address* --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 October 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-31* is/are pending in the application.

4a) Of the above claim(s) *12-31* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-11* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *22 February 2002* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *61103*.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Preliminary Amendments

1) Acknowledgment is made of Applicant's preliminary amendments filed 06/10/02, 06/14/02 and 05/23/03. With this, Applicant has amended the specification.

Election

2) Acknowledgment is made of Applicant's election filed 10/14/03 in response to the restriction requirement mailed 09/10/03. Applicant has elected invention I, claims 1-11, with traverse. Applicant's traversal is on the grounds that the claimed product is closely related to the method of making and using the product. Applicant cites MPEP 803 and argues that restriction requirements are optional in all cases, and that if the search and examination can be made without a serious burden, examination must be done on the merits even though it arguably may include claims to distinct or independent inventions. Applicant asserts that inventions I, II, IV and VI can be efficiently and effectively searched in a single search since the claims therein are grouped under the same class 435.

Applicant's arguments have been carefully considered, but are non-persuasive. In the instant case, the restriction requirement follows all appropriate statutes and regulatory principles and conforms closely with guidelines provided by MPEP, Chapter 800. Applicant is correct in that restrictions are optional. With regard to burden, MPEP 803 states that restriction is proper between patentably distinct inventions where the inventions are (1) independent or distinct as claimed, and (2) a serious search *and examination* burden is placed on the Examiner if restriction is not required. Applicants are correct that the term "distinct" is defined to mean that two or more subjects as disclosed are related, for example, as product and method of use, but are capable of separate manufacture, use or sale as claimed, and are patentable over each other (MPEP 802.01). However, in the instant case, the product of invention I is capable of separate use, i.e., as a source of coating antigenic reagent in an *in vitro* immunological assay to detect sialic acid-specific antibodies. Applicants have not presented any arguments showing that the claimed product cannot be used in a materially different non-immunization process. With regard to burden of search and examination, MPEP 803 states that a burden can be shown if the Examiner shows either separate classification, different filed of search **or** separate status in the art. In the instant application, a burden has been

established by showing that inventions I and II are classified under separate subclasses necessitating separate and non-coextensive searches of issued US patents under different subclasses. Applicants should note that divergent classification or subclassification has traditionally been utilized as one indicator that burden exists sufficient to warrant restriction. The classification system has no statutory recognition as to whether inventions are independent and distinct. For example, each class and subclass is comprised of numerous completely independent and distinct patented inventions. Further, it should be noted that the non-patent literature search, particularly in this art, is non-coextensive. Clearly, different searches and issues are involved in the examination of each invention. For these reasons, the restriction set forth in the Office Action mailed 09/10/03 is proper and is hereby made FINAL.

Since Applicant has elected the product claims of invention I, the method of using the product claims of invention IV would be kept pending pursuant to the rejoinder provisions of M.P.E.P 821.04 and would be rejoined with the elected product claims if and when the latter were deemed allowable. *Process claims that depend from or otherwise include all the limitations of the patentable product* will be entered as a matter of right if the amendment is presented prior to final rejection or allowance, whichever is earlier. Amendments submitted after final rejection are governed by 37 C.F.R 1.116; amendments submitted after allowance are governed by 37 C.F.R 1.312. The requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 C.F.R 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. § 101, 102, 103 and 112. Withdrawn process claims that are not commensurate in scope with an allowed product claim will not be rejoined. See 'Guidance on Treatment of Product and Process Claims in light of *In re Ochiai*, *In re Brouwer* and 35 U.S.C § 103(b),' 1184 O.G. 86 (March 26, 1996). Additionally, in order to retain the right to rejoinder in accordance with the above policy, Applicant is advised that the process claims should be amended during prosecution either to maintain dependency on the product claims or to otherwise include the limitations of the product claims. Failure to do so may result in a loss of the right rejoinder.

Status of Claims

3) Claims 1-31 are pending.

Claims 12-31 are withdrawn from consideration as being directed to non-elected inventions. See 37 C.F.R 1.142(b) and M.P.E.P § 821.03.

Elected claims 1-11 are under examination. A First Action on the Merits on these claims is issued.

Sequence Listing

4) Acknowledgment is made of Applicants' submission of raw sequence listing and CRF which have been entered on 06/17/02.

Information Disclosure Statement

5) Acknowledgment is made of Applicants' Information Disclosure Statement filed 06/11/03. The information referred to therein has been considered and a signed copy is attached to this Office Action.

Drawings

6) The drawings submitted in the instant application are objected to. Figure 1 has five different panels, which should be labeled as Figure 1A, 1B, 1C, 1D and 1E. Similarly, Figure 3 has two panels, which should be labeled as Figure 3A and 3B.

Priority

7) The instant application claims domestic priority to the provisional application, 60/271,044 filed 02/23/01.

Specification

8) The specification is objected to for the following reasons:

Figures 1 and 5 are incorrectly numbered. The different panels in the Figures should be individually renumbered. For example, Figure 1 has five panels and Figure 3 has 2 panels, which should be referred to as Figures 1A-1E and Figures 3A and 3B respectively. Individual Figure descriptions in the specification should be amended accordingly. All references to these Figures in the specification should be amended to reflect these changes in numbering.

Rejection(s) under 35 U.S.C § 112, Second Paragraph

9) The following is a quotation of the second paragraph of 35 U.S.C. § 112:

> The specification shall conclude one or more claims particularly pointing out and distinctly claiming the subject matter which the Applicant regards as his/her invention.

10) Claims 1-11 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention.

(a) Claim 4 is vague and indefinite in the use of an abbreviation in the claim language: 'MDCK', because it is unclear what does this stand for. It is suggested that Applicant use the full terminology at first occurrence with the abbreviation retained within the parentheses.

(b) Claim 1 is vague and indefinite in the recitation 'which supports efficient influenza virus replication' (see line 3), because it is unclear whether the term 'which' is referring to the wild-type cell or the mutant cell. If the reference is to the mutant cell, Applicant should consider replacing the recitation with --, wherein said mutant cell supports efficient influenza virus replication--.

(c) Claims 2-11, which depend directly or indirectly from claim 1, are also rejected as being indefinite because of the indefiniteness or vagueness identified above in the base claim.

Rejection(s) under 35 U.S.C § 112, First Paragraph

11) Claims 1-3 and 5-11 are rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

It is noted that the claimed mutant cell comprising decreased levels of sialic acid-containing host cell receptors for influenza virus does not exist independent of its function. The specification discloses viral propagation applications for the claimed product. The term 'mutant cell' encompasses mammalian and non-mammalian cells. The term 'mammalian cell' encompasses a myriad of mammalian cells, including human cells. However, other than a mutant MDCK canine cell, i.e., MaKS cell, having decreased levels of N-acetylneuraminic acid and N-glycolylneuraminic acid compared to the parent cell line, MDCK (see pages 19 and 20), the instant specification fails to teach any other mammalian cell, including a bovine cell, swine cell, simian cell, mink cell, or mink lung cell having decreased levels of N-acetylneuraminic acid and N-glycolylneuraminic acid compared to their respective parent cell line and the ability to support efficient virus replication. Viral propagation

applications minimally require an ability for the claimed mutant cell to support influenza virus replication. The precise structure or relevant identifying characteristics of each mutant cell that contains decreased levels of sialic acid, N-acetylneuraminic acid or N-glycolylneuraminic acid, or both, and having the ability to support efficient influenza virus replication can only be determined empirically by actually making every mutant cell that has such properties and functions, and determining whether it supports influenza viral propagation. The *Written Description Guidelines* state:

> There is an inverse correlation between the level of predictability in the art and the amount of disclosure necessary to satisfy the written description requirement. For example, if there is a well-established correlation between the structure and function in the art, one skilled in the art will be able to reasonably predict the complete structure of the claimed invention from its function.

A mere statement that the invention includes a 'mutant cell' or 'mutant mammalian cell' having the recited properties or functions is insufficient to meet the adequate written description requirement of the claimed invention. The structure of the mutant cell having decreased levels of a specific sialic acid and the recited specific biologic properties is dictated by the process of mutation and the structural changes brought by the mutation. A convincing structure-function relationship has to exist between the structure of the cell and the function of the cell produced as a result of the mutation. The function cannot be predicted from the modification of the structure induced by mutation. Whether or not cells originating from every mammalian or non-mammalian source results in the same structural changes and to the same degree is not predictable. Applicants have not shown that mutation of a reference mammalian or non-mammalian cell would automatically predict the production of a mutant cell having decreased levels of specific sialic acids and specific biologic properties, in the instant case, the ability to support efficient influenza virus replication. This is critical in light of the Applicant-acknowledged functional unpredictability. The specification at lines 13-16 on page 24 acknowledges this unpredictability in the statement that although cell lines similar to MaKS cell line have been produced in the art by Ray *et al.* (1991), such mutant cells have **not** proven useful because of their inability to support efficient influenza virus. The instant specification fails to teach the structure or relevant identifying characteristics of a representative number of 'mutant cells' from a representative number of mammals and non-mammals as recited, all having the recited properties *and* function(s), sufficient to allow one skilled in the art to determine that the

inventors had possession of the invention as claimed. What precise mutation in a generic 'cell' would lead to the recited structural and functional features is not adequately described. With the exception of a canine cell derived from MDCK, i.e., MaKS cell, a skilled artisan cannot envision the detailed structure or extent of mutation of all the mutant cell species encompassed by the recited molecule. Regardless of the complexity or simplicity of the method of isolation, conception cannot be achieved until reduction to practice has occurred. Adequate written description requires more than a mere statement that its is a part of the invention and a reference to a potential method of isolating it. The mutant cell having the recited structural and functional properties itself is required. See *Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993)* and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016.*

Rejection(s) under 35 U.S.C. § 102

12) The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office Action:

> A person shall be entitled to a patent unless –
> **(b)** the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

13) Claims 1-4 and 8 are rejected under 35 U.S.C. § 102(b) as being anticipated by Martin *et al.* (*Virology* 241: 101-111, 1998) or Brandli *et al.* (*J. Biol. Chem.* 263: 16283-16290, 1988).

Martin *et al.* taught isolated mutant MDCK RCA^r (Madin-Darby canine kidney) cells that have 70-75% reduced levels of cell surface sialic acid receptors specific for influenza virus. The mutant cells were susceptible to infection by influenza virus (see abstract; page 106; and Figures 4 and 5).

Brandli *et al.* taught isolated mutant MDCK (Madin-Darby canine kidney) cells that have 70-75% reduction in sialic acid receptors (see abstract; Experimental Procedures; Results; and pages 16286 and 16287).

Claims 1-4 and 8 are anticipated by Martin *et al.* or Brandli *et al.*

Objection(s)

14) For clarity, in line 1 of claim1, it is suggested that Applicants replace the recitation 'sialic acid containing host cell' with --sialic acid-containing host cell--..

Remarks

15) Claims 1-11 stand rejected.

16) Papers related to this application may be submitted to Group 1600, AU 1645 by facsimile transmission. Papers should be transmitted via the PTO Fax Center located in Crystal Mall 1. The transmission of such papers by facsimile must conform with the notice published in the Official Gazette, 1096 OG 30, November 15, 1989. The TC 1600 facsimile center receives transmissions 24 hours a day and 7 days a week. The RightFax number for submission of before-final amendments is (703) 872-9306. The RightFax number for submission of after-final amendments is (703) 872-9307.

17) Any inquiry concerning this communication or earlier communications from the Examiner should be directed to S. Devi, Ph.D., whose telephone number until January 2004 is (703) 308-9347 and (571) 272-0854 beginning February 2004. The Examiner can normally be reached on Monday to Friday from 7.45 a.m. to 4.15 p.m. except one day each bi-week, which would be disclosed on the Examiner's voice mail system. A message may be left on the Examiner's voice mail system.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Lynette Smith, can be reached on (703) 308-3909.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

January, 2004

S. DEVI, PH.D.
PRIMARY EXAMINER